Study the role of image guided biopsy in the management of T1 renal masses

A dissertation submitted to The Dr. M.G.R. Medical University, Tamilnadu, in partial fulfillment of the requirements for M.Ch. Branch-IV (Genitourinary surgery) examination to be held in August 2014

DEPARTMENT OF UROLOGY
CHRISTIAN MEDICAL COLLEGE, VELLORE

1 BONAFIDE CERTIFICATE

This is to certify that the work presented in this dissertation titled "**Study the role of image guided biopsy in the management of T1 renal masses**" done towards fulfilment of the requirements of the **Tamil Nadu Dr. M.G.R. Medical University, Chennai for the M.Ch (Branch– IV) (Urology)** exams to be conducted in August 2014, is a bonafide work of the candidate **Dr. Amit V Deshpande**, Senior Post graduate student in the Department of Urology, Christian Medical College, Vellore under my guidance and supervision. This dissertation has not been submitted, fully or in part to any other board or University.

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CONTENTS

Abbreviation

SRM	Small renal mass
RMS:	Renal mass biopsy
IGB:	Image guided biopsy
RFA:	Radiofrequency ablation
AML:	Angimyolipoma
RCC:	Renal cell carcinoma
US:	Ultrasound
MRI:	Magnetic resonance imaging
CT:	Computer tomography
FISH:	Flourescent in situ hybridisation
DNA:	Deoxy ribonucleic acid
VEGF	Vascular endothelial growth factor
VHL	Von hipple Lindu
FNAC	Fine needle aspiration cytology
IHC	Immunohistochemistry

ABSTRACT

TITLE OF THE ABSTRACT : To study the role of image guided biopsy in the management of T1 renal masses

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AIM / OBJECTIVES:

The aim of our study was to compare imaging guided biopsy outcome with final histopathological outcome .We aimed to calculate sensitivity, specificity positive predictive value, accuracy in determining the diagnosis.

MATERIAL AND METHODS:

We included all patients with renal mass <= 7 cm. We excluded patients with metastatic disease, patients who are not willing, with deranged coagulation profile and tumour > than 7 cm. Patients underwent image guided percutaneous renal mass biopsy. Post biopsy patients were monitored at regular interval to rule out any occult bleed, trauma to surrounding organs. The patients were provided analgesics as per need. Irrespective of the biopsy report these patient underwent surgery. The pathological characteristic of the biopsy and the histopathological specimen were compared on the basis pathological finding (malignant/benign lesion), in case of malignancy Furhann's classification.

RESULTS:

Out of 25 biopsies, 20 biopsies showed RCC, this corresponded with final histological outcome. 3 patients were reported to have hybrid oncocytolytic variant; 2 patients had oncocytoma and the third one had chromophobe RCC. 2 samples were inadequate for interpretation; the final histopathology revealed lipid poor angiomyolipoma and clear cell RCC. Sensitivities, specificities, PPVs, and NPVs for the detection of malignancy by core biopsy are 92%, 100%, 10%, 33% respectively. The accuracy of the core biopsy is 100% however the accuracy for the differentiation of Fuhrman grade was 76%.

CONCLUSIONS:

The role of RMB in the setting of T 1 renal masses is expanding. Approximately 12% of renal masses removed by surgical excision have benign pathology hence surgery can be safely differed if we know pathology beforehand using IGB. It has high sensitivity, specificity and accuracy in detecting histology of renal masses. The specific and negative predictive values are 100% and 66% relatively. Post procedure complications are relatively uncommon, encouraging us for its wider adoption.

Key words: Image guided biopsy, T1 renal masses, final histology, Sensitivity, specificity

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Introduction

In the last 20 yrs there is 2% annual increase in the incidence of renal cell carcinoma (RCC) has been observed both in Europe and in North America (1–3).The increasing incidence of RCC has occurred across all clinical stages, but the greatest increase has been observed in the incidence of localized tumors. Most of these patients were diagnosed incidentally during imaging for nonspecific abdominal or musculoskeletal complaints or follow-up of other unrelated malignancies(4).

A SMALL RENAL MASS is generally defined as a contrast-enhancing mass within the kidney with the largest dimension of up to 4 cm(4)(5) . In more recent years, 48 to 66% of RCCs have been detected incidentally as SRMs in asymptomatic patients, whereas historically most cases were diagnosed following investigations for flank pain or hematuria(6). The largest increase in incidentally detected renal tumors has occurred among patients aged 70–89 years, presumably because these individuals are more likely to undergo radiologic examination for other medical issues (7). Tumor size at diagnosis has also decreased substantially over time. (8,9)

The standard of care for small localized renal neoplasms is partial or radical nephrectomy. Progress in technology has recently led to effective minimally invasive surgical approaches for renal tumour excision, including laparoscopy and robotic assisted surgery. Those patients who are deemed surgically unfit can be considered for other non surgical approaches like cryo ablation, radio frequency ablation, HIFU or microwave therapy.

However, the histologic features of SRMs are heterogeneous. Frank *et al*(10) observed that as tumor size decreases there is a significant increase in the likelihood of a benign histology, a papillary compared to a clear-cell histology and a low-grade compared to a high-

grade malignancy. In their experience, 30% of tumors below 4 cm in their maximum dimension were benign and over 87% of those diagnosed as clear-cell RCCs were low-grade tumors. A very few small renal tumours harbour aggressive disease. An analysis of the Surveillance Epidemiology and End Results (SEER) database from 1998 to 2003 showed a 5.2% prevalence of metastasis at presentation among 8792 patients with RCCs _4 cm, with an increase of metastasis by 3.5% for each 1-cm increase in tumour size(11). On the other hand, approximately 20–25% of radiologically suspicious SRMs are benign. Although most contrast-enhancing renal masses are malignant, CT or MRI features fails to conclusively differentiate RCCs from benign tumours such as oncocytomas “low fat” angiomyolipoma.(12,13) . Moreover, a significant proportion of histologically confirmed RCCs are low-grade tumours with relatively indolent biologic and clinical behaviour (7,9).

These observations have led to the development of alternative treatment options for selected patients with medical co-morbidities, including minimally invasive ablative therapies and active surveillance (AS).However measuring the growth rate of lesions using serial radiographies has also been insufficient to predict the true natural history of renal

As a consequence, biologic data are needed to assess the natural history of either untreated renal masses under active surveillance or when energy ablative techniques. Today, the challenges in the adequate diagnosis and treatment of small renal tumors include the identification of tumors with less aggressive potential, treating less aggressive tumors less invasively and certifying tumor control after less invasive therapy. To this end, image-guided biopsy could provide information that may be helpful when deciding on the most appropriate management strategy for these patients.

Aims and objectives

The selective use of percutaneous biopsy for diagnosis in renal masses is a relatively uncommon approach when compared to the management of other solid neoplasms. With recent advancements in imaging techniques and their widespread use, the internist tumour has gone a paradigm shift and now called as radiologist's tumour. Incidental discovery of asymptomatic, small renal masses (SRM) is on the rise and a substantial percentage of these SRM are benign. Recent advances in diagnostics have significantly improved accuracy rates of renal mass biopsy (RMB), making it a potentially powerful tool in the management of SRM. RMB may offer important information enabling treating clinicians to better risk-stratify patients and ultimately provide a more personalized treatment approach for T1 renal masses.

The aim of our study was to compare imaging guided biopsy outcome with final histopathological outcome like pathological finding (malignant/benign lesion), in case of malignancy Furhann's grade. We aimed to calculate sensitivity, specificity positive predictive value, accuracy in determining the diagnosis.

Secondary outcome includes assessing the complication secondary to IGB and stratifying then between minor and major complications. We also wish to see if the nephrometry score bears any outcome on biopsy.

Review of literature

Over the last two decades, there is increase in incidence of kidney cancer worldwide. Renal cancers are responsible for 2% of all the cancer deaths in the US. This is partially due to the increasing use of non invasive abdominal imaging techniques such as US, CT and MRI. Moreover, with advances in the current imaging modalities this detection of tumour occur at very early stage (1, 2). It is estimated that renal mass is incidentally detected in around 13–26% of abdominal imaging studies. As the incidence of both benign and malignant lesions has increased, at the same time there is decrease in tumor size at the time of detection(6,16). They are usually associated with improved survival and only some of them could be potentially threatening (6, 9).

Usually simple cysts and angiomyolipomas [AML] can be diagnosed radiographically, however, many renal masses, including oncocytomas (9), atypical AML (7) and most RCC (7, 13) are not easily distinguishable on imaging and final diagnosis depends upon histopathological examination.

Presently the standard of care for such masses is either partial nephrectomy or radical nephrectomy. Early surgical intervention is justified to prevent tumour progression and improved survival. Nephron-sparing surgery is preferred as compare to radical nephrectomy for smaller RCCs, as it gives equivalent cancer-control rate and reduced progression to chronic kidney disease (14,17).At present partial nephrectomy is considered the treatment of choice for majority of clinical T1 renal masses, even in those with a normal contralateral kidney (18). With the advances in the field of minimally invasive surgery, laparoscopic and robotic partial nephrectomy, have achieved equivalent oncologic outcomes and have improved morbidity profile.

However, despite aggressive surgical resection the is hardly any change in mortality rates (19). Natural history of SRM has shown that these groups of patients have heterogeneous disease process. They have different histological subtype and aggressiveness. Only 20% of the lesions are potentially aggressive, 20% have benign histology, while the rest 60% represent indolent RCC (20, 21). Hence active surveillance was proposed as one of the option in management of SRM. Initially this approach was considered only for the patients with significant co-morbidities who are unfit for surgical intervention or elderly patients. Even though the studies on active surveillance have shown that there no progression to metastatic disease, the mean follow up in all these studies was short and hence for further validation long duration follow-up is needed(22, 23).

It was proposed that tumor growth rate can be a useful tool to assess the aggressiveness of tumour. But the natural history of SRM has shown that growth rate is very slow with only small proportion of these tumours grow significantly over time.

With the advent of RFA or cryo ablation, these patients can also be considered for minimal invasive intervention. However, there is a small but definite risk of tumor progression and metastasis.

Till last decade, the utilization of renal mass biopsy (RMB) for diagnosis of renal masses is a relatively uncommon approach when compared to management of other neoplasms. In most other solid tumors, obtaining a biopsy is one of the first steps in management algorithm. Historically, renal mass biopsy has been reserved for a limited number of indications like metastatic disease, infection, and lymphoma (24). However in the recent past, there is resurgence of renal mass biopsy (RMB). Biopsy using thin needles [20 gauge or thinner] has

been shown to be accurate in the diagnosis of renal masses (25,26) due to advances in cytological techniques (27–31) and in some cases, determination of subtype of RCC and nuclear grade(27,30).

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Technical Considerations

Imaging modality for RMB

RMB is usually done under image guidance either ultrasound [US], or computed tomography [CT] or a combination of the two. Each technique has its own distinct advantages in relation to tumor site, body habitus and other important considerations. The primary advantages of ultrasound guided biopsy are; it can be done under real time with multiplanar imaging ,it is cheap, portable and does not involve any ionizing radiations (3, 32).

However US may fail to differentiate isoechoic renal masses from normal renal parenchyma, distinguishing adjacent pleura and hollow viscera. And technical difficulties include performing biopsy in the obese population. (33)

This phenomenon could explain the high failure rate in small tumors. He suggested use of CT fluoroscopy during biopsy of such masses.

Recent advances in software and instruments allow fusion of prior CT or MR imaging to real-time US images. This combines the benefits of each modality and overcome some of the shortcoming of individual imaging (36). However , more studies are needed for validation of the technology(36).MRI can also be used to guide IGB, mostly before MRI guided thermal therapy(37).

Technique of FNAC/ IGB

Fine needle aspiration cytology

FNAC is done using mechanical disruption and suction pressure which theoretically produce more cellular samples than biopsy. Zajelda's technique uses fine needle capillary technique without suction. It results in fewer cellular smears (42). Samples can also be used to prepare cell blocks that can be used to perform specialized tests such as immunohistochemistry, FISH, and cytometric techniques(35). Cytopathologist is always required to assess sample quality and rapid handling of sample to avoid coagulum formation as it can affect the sample reporting. Skills of the cytologist is a major factor that determines diagnostic accuracy of FNA (33,43), and is mostly considered to be lower than IGB(35). Schieven LW et al (44) have showed that the processing technique has impact on the accuracy rates. Recent studies have shown that the diagnostic accuracy of FNA is reaching as high as 100% for malignant neoplasm and 92% for histological subtype(35). Masoom S et al (40) have reported an excellent concordance between FNAC and the final surgical pathology.

Core biopsy

Renal mass biopsy has its distinct advantages over cytology. Majority of the studies using the large and fine needles do not assess the performance of needle individually. Thinner needles [20 gauge or more] reduces the risk of infection, hemorrhage; even if the needle path passes through the hallow viscera or vascular organs, or the patient has impaired coagulation. By default, FNA techniques use fine needles [21 gauge or smaller].It reduces blood contamination and maximize cell yield. Fine needle aspiration is safer when there is possibility

that the biopsy tract might pass through bowel or vascular organ. The processing of sample is quicker and allows early determination of adequacy of sampling(38,39). In absence of proper RCT, most authors advise to use 18-gauge needle in order to improve the biopsy yield without increasing the procedure related morbidity (24). Breda et al in its *ex vivo* biopsy and Schmidbauer in its in *vivo* study (34) found that an 18-gauge needle was most accurate in determining histological diagnosis (45).

IGB requires fixation and pathological processing, which usually takes longer time. A frozen section may be considered but it requires specialised staff. It also has limitations with respect to accuracy (38).

Use of coaxial guide or cannula is advised while performing core biopsy. Use of coaxial guide at the extra thoracic site has reported a significant increase in the biopsy outcome without increase in morbidity (40). The coaxial technique allows multiple needle insertion of biopsy needle through the mass with only one pass through the intervening normal tissues. It minimises the chance of needle tract seedling, decreases patient's distress and reduces procedure time. The coaxial cannulas are easily seen on imaging than conventional needles. (41).

For tumors <4 cm, at least 2 biopsies from both the central and peripheral regions are recommended. For tumours more than 4 cm, two to three peripheral biopsies are advocated especially in the presence of central necrosis. Adequate core length recommended is at least 1cm (35). Each Core should be looked for size and quality. If the core appears small [<1 cm] or fragmented, an additional biopsy should be taken (35). Samples for DNA expression microarrays or genomic hybridization can be obtained (36).

Studies comparing the outcome of IGB with FNA have shown that FNA had a high rate of non-diagnostic samples and required an experienced cytopathologist for interpretation (34).

Core biopsies and fine needle aspiration appear to be interrelated. In complex cystic masses, biopsy taken from suspicious solid areas are likely to improve the diagnostic accuracy of FNA alone (24, 51). Soft, high grade tumors often provides high tissue yield during FNA because of use of negative pressure. But core biopsy is difficult because the tumor does not gel together to allow needle extraction. Wood et al (8) have reported 95% accuracy and 93% sensitivity for malignancy using a combination of both FNA and IGB.

In summary, although IGB is considered to give more accurate information in most studies, FNA can be additive to IGB and has distinct advantages in certain clinical settings.

Accuracy and false-negative results

Accuracy is defined as the percentage of positive biopsies for which the pathological diagnosis appeared to be correct; based either on the final surgical pathology or imaging surveillance. This definition is not fully correct because it considers that imaging surveillance is accurate. In a recent meta analysis by Lane et al (48), the "diagnostic accuracy" of IGB for cancer was reported to be increasing from an average of 82% before 2001 to 90% between 2001 and 2006 and recently reported to be more than 95% (40,49,50).

The **sensitivity** is defined as ratio of the number of malignancies identified by IGB to the total number of malignancy. The diagnostic accuracy of IGB as reported in literature ranges from 93 to 100 % [Table 2] whiles the sensitivity varies from 84% to 100% [Table 2]. Sensitivity is less than "accuracy", because it takes into consideration negative biopsies.

Most of these studies have reported very low false-positive rate (34, 49, 53, 54, 55) which implies that a diagnosis of malignancy on IGB can be mostly accurate and most of the time will match with final surgical pathology. In a study by Liu et al (28), the reported negative predictive value was approximately 80–90%. However, limited data is available on the negative predictive value as most of the studies are on active surveillance or patients with a benign tumour on IGB will not undergo surgery. Similarly, the data on specificity of results of IGB is also limited due to absence of surgical confirmation in many studies.

The issue of non informative biopsies is one of the subjects of concern. **Biopsy failure** represents that biopsy in which the tumor tissue could not be retrieved. **Indeterminate biopsies** included cases in which tumor tissue was retrieved, but it is inadequate for the pathologist to make final conclusion.

To standardize reporting, all biopsies are classified into four basic categories; non informative or and informative biopsy. The informative includes those that are confirmed accurate, presumed accurate or confirmed inaccurate.

In summary IGB is trust worthy owing to high sensitivity and positive predictive value of IGB and the low false negative rates. However, the major drawback includes sampling error, tumor heterogeneity, and presence of “oncocytic neoplasm” continues to exist. Thus, around 10–20% of all IGB may still represent non-informative and have to be handled cautiously.

Non informative biopsy:

It includes both biopsy failure and indeterminate biopsies. The average rate of non conclusive biopsies has been around 10–20%. In the past, many non-conclusive biopsies which

were inaccurately considered as “false-negative” were actually inappropriate biopsy. Patients with non-conclusive biopsy can undergo repeat biopsy or surgical extirpation.

The rate of indeterminate biopsies is affected by inter observer variation of pathologist and their ability to assess the amount of material required for diagnosis. Dechet et al(60) reported zero failure rate but he also observed the rate of indeterminate discordant biopsy for the two pathologists were 11 and 17%. For the IGB, the rate of biopsy failure ranged from 8 to 16% and the rate of non-informative biopsy ranged from 0 to 8% (40).

Definition of diagnostic and non diagnostic biopsies is different in different studies. In Some studies reported biopsies containing normal kidney or fibrous tissue as diagnostic and classified as the benign result (50), whereas in others, they are considered as indeterminate. So to standardize the reporting of IGB Shannon et al (61) has proposed a strict criteria for a non-diagnostic biopsy.

A biopsy is considered non-diagnostic when either there is insufficient material for analysis or sample have only normal renal parenchyma or fat or fibro-fatty connective tissue or necrotic tissue or a blood clot or with only inflammatory or fibrotic tissue.

Frequently, the sample classified as non-diagnostic biopsies contains normal renal parenchyma. The literature has shown that if repeat biopsy or surgery is performed on such patients most of then turn out to be malignant lesion [Table 1].As seen below about half of the patient with non diagnostic biopsy underwent surgery or re biopsy and about 66% of then turn out to be malignant lesion.

Table 1

Series	No. of biopsies	Nondiagnostic biopsies	Re-biopsy/surgery	Malignancy
Volpe et al (49)	100	16 non diagnostic	2 re biopsy	1 RCC
Schmidbauer et al (34)	70	9 non diagnostic	1 re biopsy 5 surgery	1 RCC 3RCC
Lechevallier et al. (24)	73	15	4 Re biopsy 3 Surgery	3 RCC 3 RCC
Neuzellet et al(35)	88	3 Failed 5 inconclusive	2 Surgery 3 surgery	2RCC 3 RCC
Shannon et al(61)	235	50 non diagnostic	12 Re biopsy 10 Surgery	5Rcc+1TCC 7Rcc+1TCC

Diagnostic and confirmed accurate biopsy

These include either confirmed-positive or confirmed negative biopsies, which have been proven by surgical excision. They represent expected outcome form IGB [Table2].

Table 2

Reference No.	No. tumors	biopsy failure **(%)**	No. indeterminate **(%)**	No. biopsy non-informative **(%)**	No. false negatives **(%)**	No. false positives (%)	No. accurate/Total No. (%)			Sensitivity for malignancy (%)
							Malignant *vs* benign	Histology	Grade	
Vasudevan *et al*. (2006) (52)	100	NA	NA	29(29%)	0	0	71/71 (100)	44/44 (100)	NA	43/51(84.3%)
Beland *et al*.(2007) (53)	58	3(5.2)	3(5.2)	6 (10.4%)	1 (1.9%)	0	51/52 (98%)	NA	NA	38/39(97.4%)
Schmidbauer *et al*. (2008) (34)	78	0	2 (3%)	2(3%)	3 (3.8%)	0	73/76 (96.1%)	59/60 (98.3%)	44/58 (76%)	60/65 (92.3%)
Volpe *et al*. (2008) (49)	100	8 (8%)	8 (8%)	16 (16%)	**0**	**0**	84/84 (100%)	56/60 (93%) for RCCs	41/60 (68%)	66/67 (98.5%)
Masoom *et al*. (2009) (55)	31	0	0	0	**0**	1 (3.2%)	30/31 (96.7%)	28/29 (96.6%)	NA	28/28 (100%)

Informative but proven inaccurate

In these samples the diagnosis on the biopsy does not match with final outcome. This group represents both false-negative and false-positive results, and is considered worrisome for clinicians. In the recent studies, the proportion of these cases was less than 1 % [Table 2]. False-negative results are of concerns, since those patients with presumed benign lesion may be lost to follow up and there is chance of spread of malignancy. The most common reasons y are the sampling error and tumor heterogeneity(53). Gupta et al have reported a lower sensitivity of 56% and a higher rate of biopsy failure in small masses owing to the technical difficulty in targeting these lesions (29).In larger tumors it can be because of the presence of central necrosis(29, 54). Most renal masses are known to demonstrate a varied degree of tumor

heterogeneity usually up to 25%, thus complicating the situation even further(55,56,57). Finally, there exists interobserver and intraobserver variability amongst pathologists which complicates the picture (46, 47).

Informative and presumed true

The lesion is differentiated as a benign lesion from a malignant one; however lack pathological confirmation. This group represents of about approximately 20–37% of all cases as shown in table 2. Most of the patients with IGB showing benign lesion were managed with close surveillance with clinical examination and radiological investigations. However, without a comparable surgical histology, this presumed diagnosis cannot be authenticated. In a study by Schmidbauer et al, 78 patients with renal masses underwent biopsy and then subsequent surgical excision. 21 patients had a benign diagnosis on biopsy (34), however after the final histology, 3 patients were found to have a malignant tumour thus representing false-negative result. “Oncocytic neoplasms” on IGB needs special mention as typically they were considered to be benign at many centers. But this group comprises of both benign and malignant lesion and requires special immunohistochemical markers for further differentiation. Thus, the final management of a patient with a lesion with a benign biopsy result will depend on the multiple factors such as radiographic appearance of the lesion, patients’ age, co morbidities and patient’s preference.

Accuracy of tumor grade and subtype

Fuhrman grading of RCC is classified on the basis of nuclear size, shape, and nucleolar prominence. In spite of its widespread use, the prognostic significance and reproducibility have also been questioned. Most pathologists depend upon assessment of nucleolar prominence alone while grading renal cell carcinoma. Delahunt B et al (111) have shown that worst the nucleolar grade, worst is the outcome in relation to aggressiveness of cancer.

With increasing sophistication of IGB, there has been renewed attention to Fuhrman grading of biopsies, so as stratify tumor risk behaviour. In literature, for Fuhrman nuclear grade the similarity between the IGB specimens and post op histopathology range from 45% to 90%, although most discordant cases off by only one grade(33, 34, 54, 58). In the Lebret study, by classifying the lesion into “low” and “high” grade, he has increased the concordance rate to as high as 76%. This difference in the concordance is because of both interobserver variability and tumor heterogeneity. The significance of this concordance may be more relevant in the setting of management of these patients with active surveillance or minimally invasive ablative therapies, which are relatively contraindicated for a high-grade cancer, regardless of size(59). Similarly accuracy for identifying the histological subtype ranges from 87–100% (27).

Complications:

Complications after the imaging guided biopsy need special mention. The Society of Interventional Radiology has classified biopsy complications into minor and major categories depending on patient's outcome. Minor complications are those in which patient required no or nominal therapy in the form of overnight hospital admission for observation only. Minor complication of image guided biopsy includes biopsy site pain or localized skin hematoma.

Major complications are defined as those which require treatment or longer hospitalization, or lead to permanent adverse outcome or death. Most of these studies on IGB and FNA showed few or no major complications (62). The most common complication encountered is bleeding, which is usually subclinical and detected on CT scan during follow up with self-limiting treatment. Tang et al have reported bleeding rates of 91%, however, major bleeding requiring transfusion or hospital observation occurred in only 1.5% of cases (62).

Although theoretically it is believed that larger-needle biopsies (18 gauge or less) are associated with higher risk of bleeding complications than with smaller-needle biopsies (20 gauge or more), published studies showed no significant difference in bleeding complications based on needle size(8).

Other differential diagnosis for persistent bleeding is arteriovenous fistula. This complication rate varies from 1.5–16% of cases (62, 63). However, a majority of these are self-limiting and clinically insignificant. Majority of arteriovenous fistulae resolve on their own in a period of 3.5–20 months without any intervention (63). The remaining may present with clinical symptoms such as hematuria, hypertension or alteration in kidney function and are usually managed with angioembolization (64).

Pneumothorax can develop as a result of biopsy of upper pole renal masses from posterior aspect. It is usually clinically insignificant and rarely needs treatment. Death following renal biopsy is a rare event. Smith et al have published data of about 16,000 cases of abdominal fine needle biopsies. They have documented overall mortality rate of 0.031% (53) most common causes being hepatic hemorrhage and pancreatitis. This can almost always be prevented in all cases of kidney biopsy. Finally, there is no evidence that needle biopsy complicates subsequent surgical procedure. There are no studies available to compare the complications in US guided versus CT guided biopsies. However under CT guidance, the chance of injury to hollow as well as solid viscera is less than 1%.

The most disputed possible complication of RMB is the risk of tumor seedling along the needle tract. Only 6 cases of possible tumor dissemination from needle biopsy have been reported in the literature since 1991. The overall presumed chance of needle tract seedling is less than 0.01%. The needle size had no correlation with risk of seedling but the risk increases with use of non cutting needles and with the number of needle passes. Furthermore with the use of coaxial biopsy technique the chance of tumour seedling are negligible. (Table 3)

Table 3

References	Needle size	Time to presentation	Pathological finding
Gibbons et al(65)	18	20 months	RCC
Kiser (66)	14	24 days	Papillary RCC
Shenoy (67)	23	12 months	RCC
Abe and Saitoh (68)	14	18 months	Liposarcoma

Transitional cell carcinoma carries a higher risk of seedling than RCC. In cases presence of radiological suspicion of a renal pelvic urothelial tumor or positive urinary cytology, endoscopic rather than percutaneous biopsy is recommended.

Another often discussed potential consequence of IGB whether the IGB makes the subsequent surgical management difficult or forced us to change our surgical plan. However, increasing evidence suggests that previous biopsy does not result in increased surgical complications or negatively impact outcomes and should not be used as a reason for avoiding IGB (8, 30, 35).

Contemporary indications for renal mass biopsy:

The established indications for renal mass biopsy includes patients renal mass and known extra renal malignancy, renal mass and febrile UTI to rule out possible abscess, suspected case of lymphoma, concomitant with thermal ablation (6, 9).

A new, emerging indication includes patients with small [less than or equal to 3 cm] solid masses. Although there may be multiple indications in a given patient, only one indication may be needed to proceed with a biopsy.

Absolute indications:
Renal mass and known extra renal malignancy
Renal mass and febrile UTI, possible abscess
Suspected lymphoma
Concomitant with thermal ablation

Relative indications:
Mass in a solitary kidney or bilateral renal masses
Renal mass with imaging features suggestive of unresectable renal cancer
Medically unfit

Emerging Indications:
Small enhancing renal masses
Indeterminate cystic lesions
Determination of tumor subtype in metastatic setting

Patients with imaging findings suggestive of inoperable renal cancer

Renal cell carcinoma may be unresectable either due to locally advanced disease or distant metastases. In patients with imaging findings highly suggestive of unresectable renal cell carcinoma, biopsy is important to establish the diagnosis and offer appropriate treatment. It can be performed safely with and has a high sensitivity (54,73). When the tumor is locally advanced, the renal mass is the only possible site of biopsy. In case of metastases disease, site

of biopsy needs to be decided on the basis of risk-to-benefit analysis so as to get highest yield and the lowest risk to the patient. For example, in a patient with renal cell carcinoma with lung metastasis, obtaining a biopsy from a possible metastatic deposit to the lung may carry a risk of pneumothorax. In such a situation, the biopsy from the renal lesion may provide us better yield with less risk to patient.

Chemotherapy for renal cell carcinoma historically has been ineffective. Immunotherapy with cytokines, tyrosine kinase inhibitor or VEGF receptor inhibitor have mixed respond depending upon the tumour subtype (74). Newer agents, such as Sorafenib, Sunitinib, target vascular endothelial growth factor [VEGF] have been approved for use in metastatic clear cell carcinoma and validated in clinical trials(75,76). For non clear cell subtype recent guideline suggest use of mTOR pathway inhibitors like Tamsirulimus. Hence IGB has role in patient with unresectable renal primary (76).

Patients with known extra renal primary cancer

The commonest malignancies to metastasize to the kidney are lung and lymphoma (54,71). Metastatic lesions to the kidney are not rare; autopsy studies demonstrate renal metastases in 7-13% of patients with cancer (69,70). The identification of an enhancing renal tumour in a patient with an extra renal malignancy poses a diagnostic dilemma regarding whether the mass represents a primary renal cell malignancy or a metastatic lesion. Despite this high propensity for renal metastases, Rybicki et al (54) demonstrated that 31 of 54 renal masses in patients with extra renal malignancies represented renal cell carcinoma. Accurate

diagnosis is required because of major treatment implications i.e. most metastatic lesions require medical treatment, whereas renal cell carcinomas are resected or ablated.

The sensitivity of biopsy in this group of patients has been reported to be 90% (54). Although cross sectional imaging showing features such as bilaterality and multiplicity and fewer enhancements as compare to surrounding renal parenchyma in most probability point out towards metastases, these features can also be rarely seen in patients with renal cell carcinoma (50). Cystic masses, however, are unlikely to represent metastases (54). Sánchez-Ortiz RF et al have suggested that in patients with an extra renal malignancy and no evidence of disease elsewhere, a renal mass is almost certainly renal cell carcinoma(72), however, in patients with an extra renal malignancy and extra renal metastases, the renal mass cannot be assumed to be a metastasis.

Patients with a solid renal lesion caused by infection

Renal infections can have varied radiologic manifestations (77), rarely they may present as a tumour-like abnormality and behave like a neoplasm (78). Imaging features such as ill-defined margins on ultrasound (28) or ill-defined margins, perinephric stranding and patchy enhancement on CT (79,80) usually suggest localized infection. An infective pathology can be diagnosed with confidence if associated with clinical and laboratory signs of infection. However, in absence of signs and symptoms of a urinary infection (81), a renal mass might be treated as tumor inadvertently. This misinterpretation may lead to surgical resection rather than antibiotic therapy. In such small group of patients, in whom a mass-like abnormality may be due to an infection, percutaneous biopsy may help to provide the correct diagnosis.

Patients with co-morbidities in whom surgery is planned

The management of patients with a suspected resectable renal cell carcinoma with medical co-morbidities poses a challenging situation for the treating urologist. Co-morbidities involves mostly the lung or heart related ailments but can be associated renal insufficiency or the presence of mass in a solitary functioning kidney. A formal plan depends not only on assessing the surgical and anesthetic risk for the patient. But now with the availability of IGB we can safely differentiate renal cell carcinoma from benign neoplasm and avoid unnecessary treatment (7,13,17). In cases, where biopsy has provided a definitive diagnosis of RCC, we can plan surgery with more confidence (73).

Patients with a small [< 3 cm] hyperattenuating homogenously enhancing renal mass

Benign non enhancing entities include hemorrhagic or proteinaceous cysts, hematomas, vascular anomalies, angiomyolipomas, oncocytomas and rarely metanephric adenoma. The malignant lesions include renal cell carcinoma and lymphoma. These benign neoplasms may be difficult to differentiate from RCC by imaging alone (83–87). Roughly 5% of AMLs have no imageable fat component (12, 83-87) and typically seen on CT as small hyperattenuating masses that enhance homogenously (85). In these cases, MR imaging has a peculiar role. MR imaging allows differentiation between lipid poor AML and clear-cell carcinoma, which are hypointense (85) and hyperintense (88), respectively, on T2-weighted imaging.

The papillary RCC is more difficult to differentiate from lipid poor AML because it is also hypointense on T2-weighted imaging (89,90). Percutaneous biopsy is therefore required to differentiate AML with minimal fat and papillary RCC.

Patients with a renal mass for which percutaneous ablation is considered

The indications for renal mass ablation are becoming more diverse. Ablation is nephron-sparing and therefore useful in certain high risk patients including those with bilateral tumors, solitary kidneys and in presence of renal insufficiency (91–96). Its use is now advocated in small unilateral renal cell carcinomas as an alternative to surgical resection (97). Biopsy of a suspected renal cell carcinoma before ablation is imperative because of obvious reasons. In surgical resection, whereby the entire surgical specimen can be examined pathologically, ablation destroys the neoplasm, and thus no tissue is available for analysis post procedure. Therefore, the IGB prior to procedure provides the only opportunity for a tissue diagnosis. Furthermore, cross sectional imaging has limitation in differentiating between benign and malignant lesion (98, 99). Tuncali et al. (98) demonstrated that 37% of masses referred for ablation were benign. Treating a benign lesion with percutaneous ablation has inadvertent implications. Not only is the treatment inappropriate and exposes the patient to unnecessary risks but the patient is wrongly labeled with a diagnosis of cancer, and subjected to lifelong clinical and radiologic follow-up.

To validate the technique relative to surgery, the pathology of lesions treated must be known prospectively by pre procedural biopsy. Unfortunately several clinical trials of percutaneous ablation (93, 95) included renal masses that were diagnosed solely based on

imaging. If many of the lesions treated were in fact benign, the efficacy of ablation was overestimated.

Indeterminate cystic renal mass

The Bosniak classification of cystic renal masses is well established and widely used (1). Historically, it has stratified these masses into four broad groups. The chances of getting malignancy is 0% in types I , 5% in typed II cyst, about 50% in type III cyst and about 95% in type IV cyst(74,100). Hence historically type I and II cyst are considered as nonsurgical lesions and types III and IV are typically resected surgically (1).

Type III lesions are indeterminate and cannot be definitely diagnosed as benign on imaging alone. Although the risk of malignancy is highly variable [31-100%] resection is advocated so as not to miss a cancer. Biopsy in this group has been traditionally seen to be of limited use as false negative biopsy results are common (1). However, those patients who are not surgical candidates the biopsy may be useful (101). Rybicki et al. have demonstrated a sensitivity of IGB to be only 33% whereas Harasinghani et al (102) managed to render a diagnosis in 100% of renal cystic lesions. Given this wide spectrum of test performance, biopsy is unlikely to become routine in the diagnosis of Bosniak type III cystic lesions. It can be considered in patients with surgical co-morbidities. A malignant biopsy result allows surgery to proceed with confidence. A negative result may be definitive when a specific entity such as oncocytoma or metanephric adenoma is diagnosed. Otherwise, a negative result may provide more confidence in following patients.

Multiple solid lesions

Lymphoma, metastases are the most common conditions associated with multiple solid lesions. Clinical history and extra renal findings usually provide the clue to the diagnosis. However there are certain hereditary renal cell carcinomas which can result in multiple solid renal masses (103). A fine balance needs to be reached between successful eradication of tumour as well as preserving functioning renal tissue to avoid dialysis. Nephron-sparing techniques such as partial nephrectomy and ablation are often used in combination. Not all hereditary syndromes, however, produce malignant masses. Renal oncocytosis results in multiple oncocytomas that are benign and do not require treatment (9). Percutaneous biopsy is therefore crucial to establish the correct diagnosis before definitive treatment is undertaken (103).

Small [3 cm] solid masses

The principal criterion for determining the role of biopsy in this emerging indication is the size of the solid renal mass. Surgical data have consistently demonstrated that as the size of a solid renal mass decreases, the probability of it representing a benign entity increases (41). Benign masses most commonly resected include angiomyolipomas with minimal fat, oncocytomas, metanephric adenoma, papillary adenoma, and leiomyoma (10,104). These masses have historically undergone unnecessary surgical resection because they cannot be distinguished from malignant lesions by imaging alone. By performing biopsy of small solid renal masses, a significant proportion of benign lesions may be confirmed, obviating the need for radical surgeries. Although the size criteria for biopsy in benign etiology is not standardized,

biopsy would be more appropriate in smaller masses The masses less than 1 cm are difficult to target for biopsy.

The increasing treatment of incidentally detected small renal masses is an area of continued controversy (106). Mixed results regarding the biologic aggressiveness of small renal cell carcinomas with respect to size have been reported(15), However, consensus suggests that smaller renal cell carcinomas tend to be of lower grade and more indolent. Co-morbidities, patient preference, life expectancy and age are factors that may influence the management. The indolent natures of some small renal cell carcinomas have prompted some to consider observation in lieu of resection or ablation (107). Percutaneous biopsy can help determine the most appropriate management plan by providing information such as cell subtype and Fuhrman nuclear grade, which can be used to judge the tumor's potential for growth and metastases.

Pathological advances:

Advances in cytogenetic techniques, and the discovery of newer markers for identifying precise renal tumours, provide distinct advantage for image guided biopsies. [Table 4] (108–110). These techniques help us to reduce the rate of inderminate biopsies and help us to differentiate “oncocytic neoplasms”.

The term “oncocytic neoplasm” needs special mention. This group comprises of oncocytoma, chromophobe RCC, granular variants of clear cell RCC, eosinophilic variants of papillary RCC, and epithelioid AML. Oncocytic neoplasm remains a major diagnostic dilemma in the field as a result of overlapping cytomorphology, particularly with the limited pathological material obtained from IGB. Beland et al analyzed, inderminate IGB by conventional staining, using immunohistochemistry and other ancillary techniques, and provide conclusive diagnosis in 89% of cases (53).

Liu and Fanning analyzed 18 tumors with FNA, and are able to diagnose oncocytic neoplasm 10 patients (28). Of these patients, eight were oncocytomas [80%], one was eosinophilic papillary RCC and remaining one was chromophobe RCC on final surgical pathology. Schmidbauer et al (34) also showed similar results suggesting that 10–20% of “oncocytic neoplasms” IGB might turn out to be malignant on rigorous pathological analysis. IHC stains that are routinely used appear to have limited success in tumor diagnosis and classification in this setting (28,111)and hence there is increasing use of ancillary studies, such as FISH and electron microscopy to improve the diagnostic accuracy for “oncocytic tumors”. This has not been routinely incorporated into most of the studies till date (28,111).

Table 4

Renal cell carcinoma subtype	Histology	**Molecular markers**	**Genetic alterations [Koul et al., 2011]127**
Clear cell	Nests of tumor cells separated by thin interconnecting vasculature and dilated sinusoidal space.Tumor cells with clear cytoplasm	[+] GST-α, Vimentin,ADFP, CA-IX,EMA,LMWCK, CD10,Caveolin-1,MOC-31,CD26 [−]:K19,AMACR,Keratin7,CK20,CK7,HMWCK,Ron, Parvalbumin	−3p25, +5q22, −6q, −8p12, −9p21, −9q22, −10q, −14q
Papillary	Tumor cells forming papillary structures with foamy histiocytes and hemosiderin.	[+]:AMACR,CA-IIKeratin7,CD10,CD15,LMWCK [−]: GST-α, CA-IX,Ron,Parvalbumin	+3q, +8, −9p21, +12, −14q, +16, +17q21, +20
Chromophobe	Large and polygonal tumor cells with finely reticulated cytoplasm, prominent cell border resembling plant cells and irregular wrinkled nuclei with perinuclear clearing	[+]: CA-II,Parvalbumin,CD74,Galactin-3,Cytokeratin 7,Caveolin-1,MOC-31,CK7,E-cadherin,CD10 [−]:AMACR,K19,Vimentin,ADFP, HMWCK,Ron, CD26	−5q22, −8p, −9p23, −18q22
Oncocytoma	Nests of tumor cells with abundant eosinophilic granular cytoplasm and uniform nuclei.	[+]: CA-II,Parvalbumin,Ron,Galectin-3,CD10, LMWCK, E-cadherin, Caveolin-1, CD26 [−]: GST-α, AMACR,K19,Vimentin,CD74,HMWCK	−1p, −8p, −11q13,14q, −19q, −21q, −X/Y, der[13]t[13;16][p11;p11]
Angiomyolipoma	Classical cases with namesakecomponents: fat, abnormally formed vessels and smooth muscle cells. Tumors with predominantly one element can occur.	[+]: Melanocytic markers: HMB-45 and Melan-A [-]: Epithelial markers	None

Cost-effectiveness of renal mass biopsy

An important consideration in the discussion of renal mass biopsy is the economic impact of various treatment approaches. Heilbrun et al estimated that for a hypothetical healthy 60 year-old man with a SRM <2 cm, IGB was more cost-effective than immediate treatment for quality adjusted-life years gained(97).

After considering biopsy performance, the probability of tract seedling, possibility of growth of the SRM, treatment costs, patient out- comes, and quality of life, Pandharipande et al

(112) compared IGB to surgery or imaging surveillance. Their Markov model clearly favored IGB in term of cost-effectiveness. Thus both these studies argue in favour of IGB when faced with a SRM.

Role of imaging

Although most enhancing renal masses are malignant, there are no definitive characteristics of a renal mass on CT or MRI that can conclusively distinguish between malignant tumors from benign lesions (113). Can we solely depend on imaging information as an alternative to biopsy? Can IGB provide superior diagnostic accuracy when compared head-to-head with imaging? Dechet et al(60) conducted a study where two radiologists reviewed CT scans from 100 patients with a solid renal mass and these results were compared to those of pathologists reviewing core samples. Pathologists reviewing core biopsy rates were superior in all categories with accuracy rates of 77 and 72%, non-diagnostic rates of 20 and 21%, sensitivities of 81 and 83% and specificities of 60 and 33%. Radiologists utilizing CT imaging alone could reach to the accuracy rates of 60 and 66% with non-diagnostic rates were 31 and 23%, sensitivities were 70 and 77% and specificities were 20 and 20% for each radiologist respectively.

In a retrospective review of 543 patients who underwent surgical excision compared pre-operative imaging to final pathology, Dorffner et al found a negative malignancy rate of 14.7% and also that the mass size did not predict final pathology with 83% of benign masses considered suspicious for malignancy based upon imaging(114). When examining fine needle and core biopsies of patients presenting for percutaneous ablation, Heilbrun et al (97) found imaging has a positive predictive value of 95% for malignancy but a non-diagnostic rate of

11.8%. Unfortunately, there is no study which has head to head comparison between imaging, core biopsy and final surgical outcome. Considering the limitations of imaging alone to conclusively determine malignancy, it is clearly advantageous to perform IGB.

Material and methods

We have performed image guided biopsy of T1 renal masses and compared its outcome with the final histological outcome

P**rimary Outcome:**

- To compare imaging guided biopsy outcome with final histopathological outcome like pathological finding (malignant/benign lesion), in case of malignancy Furhann's grade.

Secondary Outcome/s:

- Sensitivity, specificity positive predictive value, accuracy in determining the diagnosis.
- Minor and major complications following the biopsy
- Age, sex and size stratification of the renal mass, renal nephrometry score and correlation of it with the final biopsy.

Key Criteria

a. Inclusion Criteria: All patient detected renal mass <= 7 cm.

b. Exclusion Criteria:

1. Metastatic disease on presentation
2. Patient who refuse to give consent.
3. Patients who have deranged coagulation profile.
4. Tumour > than 7 cm.
5. Renal vein, IVC thrombus

After institutional review board approval and the patients were recruited to undergone image guided percutaneous renal mass biopsy. The patients came for management of detected renal mass. Suitability of the patient to include into the study was confirmed as per inclusion and exclusion criteria.

Before percutaneous biopsy, blood born virus status, the platelet count of >50 000/mm3 and coagulation profile with normal limit (INR<1.3%) were confirmed.

Informed written consent was taken prior to biopsy. Details of the consent form were given in later paragraphs. All these patients were admitted for one day prior to biopsy or the biopsy is done one day prior to the final surgical procedure.

Premedication in the form of inj morphine and inj phenargan were given prior to biopsy (According to body weight, single dose, intramuscular). The patient will be placed in the prone position, and 1% lignocaine local anesthesia was used. Under Computed tomography guidance a coaxial technique was used for biopsy. The coaxial technique limits the number of times the renal capsule is violated, and it decreases the risk of bleeding. However, the needle should be allowed to move with respiration. Almost all biopsies initially involved core biopsies (2-4 cores) when the aspirate sample was sufficiently solid and cellular (usually 17 to 20 gauge. The biopsy will be processed by uro pathologist.

Post biopsy patient's vital were monitored at regular interval to rule out any occult bleed, trauma to surrounding organs like pleura, liver, colon, spleen. The patients were provided analgesics as per need. Those patients who have post biopsy complication will be transferred under urology for further management.

Irrespective of the biopsy report these patient will be offer radical /partial nephrectomy to avoid the bias.

The pathological characteristic of the biopsy and the histopathological specimen were compared on the basis pathological finding (malignant/benign lesion), in case of malignancy Furhann's classification, immunehistochemistry marker.

Definition:

Accuracy: The percentage of informative biopsies for which the pathological diagnosis appeared to be correct; that is, based on final surgical pathology

Biopsy failure was defined as any procedure for which the tumor could not be targeted or tumor tissue could not be obtained.

Indeterminate biopsies included cases in which tumor tissue was obtained, but the pathologist could not make a definitive diagnosis and could not differentiate between benign and malignant lesion.

The **sensitivity** defined as the number of cancers identified by RMB relative to the total number of cancers.

The imaging of the renal masses will help in calculating the renal nephrometry score. The efficacy of the image guided biopsy in detection of the renal masses will be studied. We also stratify the patient according to age, sex and size of tumour and determine whether these factors could predict the pathologic nature of such masses. We have compared the size of the mass on imaging with the final biopsy outcome so as identified were the imaging overestimated/underestimated the size of mass

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Proforma

To study the role of image guided biopsy in management of renal masses

Patient Details

1. Name
2. Hospital number
3. Age/Sex
4. Address
5. Comorbidities

Investigation:

1. CT finding
    I. Tumor size
    II. Location
    III. Amenable to biopsy
    IV. Nephrometry score

Details of biopsy:

1. Number of core obtained

2. Post biopsy complication

    Minor:
        i. Pain at biopsy site
        ii. Hematoma at biopsy site
    Major:
        I. Profuse Bleeding that needs further admission and blood transfusion
        II. Arterivenous fistula
        III. Pneumothorax, haemothorax

IV. Biopsy leading to complication during final surgical procedure or change of surgical plan
V. Death

Biopsy outcome:

Details of surgery:

I. Initial plan before biopsy:
II. Change of plan after biopsy:
III. Time duration of surgery
IV. Need for Vascular clamping
V. If clamping done then with or without cold ischemia
VI. Time of clamping
VII. Injury to blood vessel
VIII. Opening of Pelvicalyseal system
IX. Pleural injury
X. Peritoeum injury
XI. Trauma to surrounding organ

Final biopsy outcome

Results

The mean age of the patients was 48 yrs. (median:51 yr; range: 28–83 yr) and 4 patients (16%) were women. 84% percent of renal tumors did not have symptoms pertaining to renal masses. 84% patients had at least one co morbid factor listed in the table. Two patients had multiple tumours and one patient had bilateral tumors. 14 renal tumors were located in the left kidney (56%). (Table5).

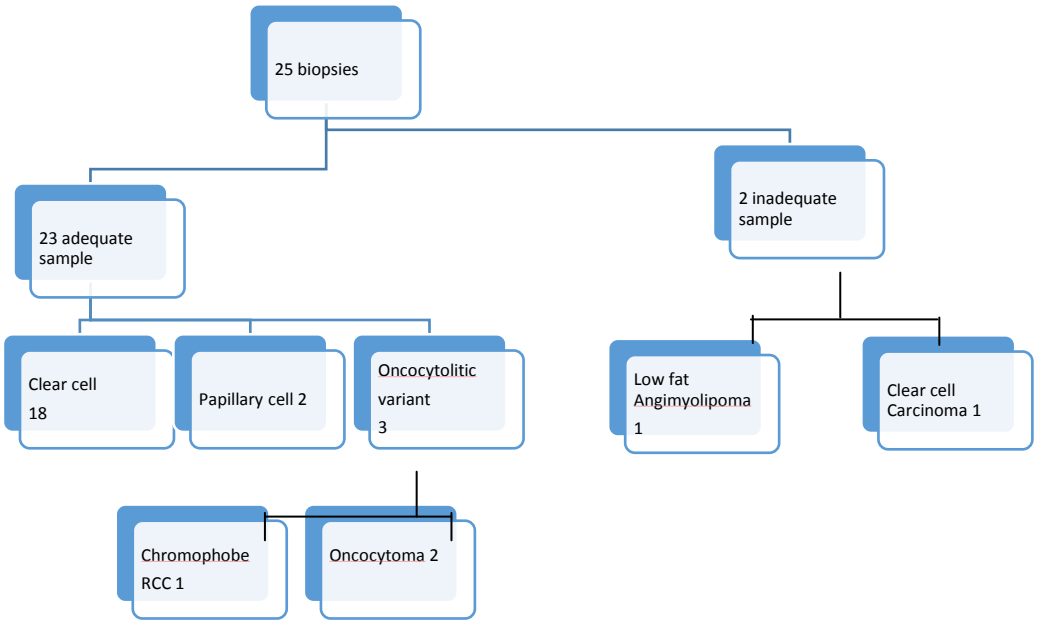
Table 5	**Demographic profile**	
Total patient		**25**
Mean Age		48.8 yr
Sex	Male	21
	Female	4
Side	Left	14
	Right	11
Co morbidities	DM	8
	HT	11
	CKD	4
	Other	13

Presentation	Non specific Flank pain	4
	Hematuria	4
	Other	3
	Incidentally detected during routine evaluation	14

Mean tumor diameter on preoperative CT scan was 4.1 cm (median: 3.2 cm; range: 2.2-7cm); About 68% tumours had size less than equal to 4 cm. Post operatively however about 88% tumours were reported as pT1a suggesting that the CT overestimates the size of tumour. We failed to identify any correlation nephrometry score with core biopsy except that 3 of the 6 patients whom radiologist refused to do biopsy were in anterior lip. (Table 6).A flowchart of the results of core biopsy is shown in table 7. Out of the 25 core biopsies, 20 biopsied showed RCC, which also correspond to final histological outcome. 3 patients were reported to have hybrid oncocytic variant, out of which 2 patients had oncocytoma and the third one turn out to be chromophobe RCC. 2 samples were inadequate for interpretation; the final histopathology revealed lipid poor angiomyolipoma and clear cell RCC respectively. (Table 7)Out of 25 core biopsies, 22 patients had malignancy in final histological outcome.1 core biopsy which was inadequate for reporting was found to have RCC. Out of the three patients in whom core biopsy revealed hybrid tumour, one was eventually found out to be chromophobe RCC.

Table 6		Biopsy
Mean CT size		4.1 cm (median: 3.2 cm; range: 2.2-7cm)
CT size	T1a T1b	17(68%) 8 (32%)
Final histopathology	T1a T1b	22 (88%) 03 (12%)
Multiple tumour		2
Bilateral tumour		1

Table 7



Considering this about 2 out of 22 patients might have been missed if biopsy was considered as final criteria.

Table 8

	Malignant
Insufficient	2(25)
Detection of malignancy (accuracy)	100%
True-positive, *n*	20
False-negative, *n*	1
False-positive, *n*	0
True-negative, *n*	2
Sensitivity	95%
Specificity	100%
PPV	100
NPV	66%
Accuracy for RCC Subtype	91%
Fuhrman grade	75%

Sensitivities, specificities, PPVs, and NPVs for the detection of RCC core biopsy are shown in table 4. Out 0f the 20 patients where biopsy revealed RCC, subtype was correctly predicted in 100% patients. However the accuracy for the differentiation of Fuhrman grade was 75% of biopsies using core biopsy. The incorrect grade was identified using core biopsy in 25 %

(n = 5). Core biopsy failed to identify Fuhrman grade 3 in 1 patients and rest 4 patients the core biopsy grade was grade I, however the final histological outcome showed Fuhrman grade II.

Discussion

As earlier mentioned, RMB is usually carried out using an 18-gauge needle to optimize the cellular yield without increase patient morbidity. For tumour less than 4cm, it is recommended to take 2 biopsies from central and peripheral zone. For tumours more than 4 cm especially if there is presence of central necrosis two to three peripheral biopsies are advocated as standard protocol. Cores should be visually assessed for size and quality. If the cores appear fragmented or particularly small [<1 cm] additional biopsies should be taken. (35). Samples can be used to extract genetic material for genomic analyses.(33) .Although there is no randomized prospective data, most author' experiences suggest that the use of an 18-gauge needle improves biopsy yield relative to FNA(24).

In this study biopsies were performed with co axial technique using 17 G cannula and 18G tru cut biopsy gun. **We are able to obtain average 3.6 adequate cores per biopsy. We have noticed that with the above protocol we are able to get adequate tissue in about 92% cases.** Breda *et al*. carried out *ex vivo* RMB and found that an 18-gauge needle [or larger] was most accurate in determining histological diagnosis (45) and Schmidbauer *et al*. reported similar findings related to their *in vivo* study(35)

Renal mass biopsy is most often done under image guidance. Each modality (US, CT) has its own distinct advantages related to tumor location, body habitus and other important considerations. The potential disadvantages of US include the inability to differentiate isoechoic renal masses from normal renal parenchyma, distinguishing adjacent pleural folds and bowel. Technical difficulties include biopsying in the obese population. (113)

All these problems can be avoided using CT fluoroscopy. The advantages of CT guidance are that 1] gas and other structures do not obscure visibility, 2] there is excellent spatial

resolution, 3] there is better needle visualization, 4] it is easier to avoid necrotic areas and 5] there is more rapid skill acquisition. 6] It also provides a higher resolution image and thereby facilitates the avoidance of adjacent vital structures and necrotic areas at the time of sampling.

Table 9

Reference	No of tumours	No pathological confirmation	Radiological surveillance	No of Cancer	biopies		Guidance	Complication	
					Needle Size	No of sample		Minor	Major
Vasudenvan(52)	100	48(48%)	43(43%)	51(51%)	16G	NA	CTorUS	0	1
Beland(53)	58	8(13.8%)	45(77%)	39(67%)	Varied	NA	CTorUS	0	0
Volpe(49)	100	21(21%)	79(79%)	67(67%)	17Gcannula 18Gbiopsy	NA	CTorUS or both	3	0
Masoom(40)	31	31(100%)	0	28(90%)	FNA	NA		NA	NA
Schimidbauer (34)	78	78(100%)	0	65(83%)	18G and FNA	2-3	CTorUS	1	0
Maturen (116)	152	87(57%)	NA	87(57%)	18G	3-4	CTorUS	1	2
Present study	**25**	**25(100%)**	**0**	**23(92%)**	**17Gcannula 18Gbiopsy**	**2-3**	**CT**	**8**	**1**

In the present study all the biopsies were done under CT guidance. We are able to obtain adequate sample in 92% cases (Table 9). By using CT fluoroscopy, which allows biopsy gun activation in real-time mode, Neuzellet et al (35) discovered that in some cases the needle pushes the tumor instead of penetrating it. This phenomenon could explain the high failure rate in small tumors observed in studies where fluoroscopy is not used. Schimidbauer(34) et al reported a study on 78 patient who underwent biopsy followed by surgical extirpation. The patient underwent FNA and biopsy both before surgery. The imaging modalities used however was not uniform**.**

Post RMB complications are always been unreported or less reported. However in general the complication rate is less than 1%. We have used the norms of The Society of Interventional Radiology for reporting the complication. Complications are classified into minor

or major depending on patient outcome. Minor complications are defined as those that require no or nominal therapy, including overnight hospital admission for observation only. Minor complication of CT guided biopsy are includes biopsy site pain, localized skin hematoma. Major complications are those that require therapy or longer hospitalization, or lead to permanent adverse sequelae or death. In the present only patient required change of original surgical plan because of perinephric adhesion and hematoma.5 of the 7 patients reported biopsy site pain

Table 10

Reference No.	No. tumors	biopsy failure **(%)**	No. indeterminate **(%)**	No. biopsy non-informative **(%)**	No. false negatives **(%)**	No. false positives (%)	No. accurate†/Total No. (%)			Sensitivity for malignancy (%)
							Malignant *vs* benign	Histology	Grade	
Vasudevan *et al*. (2006) (52)	100	NA	NA	29(29%)	0	0	71/71 (100)	44/44 (100)	NA	43/51(84.3%)
Beland *et al*.(2007) (53)	58	3(5.2)	3(5.2)	6 (10.4%)	1 (1.9%)	0	51/52 (98%)	NA	NA	38/39(97.4%)
Schmidbauer *et al*. (2008) (35)	78	0	2 (3%)	2(3%)	3 (3.8%)	0	73/76 (96.1%)	59/60 (98.3%)	44/58 (76%)	60/65 (92.3%)
Volpe *et al*. (2008(49)	100	8 (8%)	8 (8%)	16 (16%)	**0**	**0**	84/84 (100%)	56/60 (93%) for RCCs	41/60 (68%)	66/67 (98.5%)
Masoom *et al*. (2009) (40)	31	0	0	0	**0**	1 (3.2%)	30/31 (96.7%)	28/29 (96.6%)	NA	28/28 (100%)
Present Study	**25**	**2**	**3**	**0**	**1(4%)**	**0**	**22/25 (88%)**	**22/25 (88%)**	**15/20 (75%)**	**95%**

with 1 patient developed localized hematoma at biopsy site. 1 patient required admission for more than 24 hrs for monitoring.

Sensitivities, specificities and diagnostic accuracy:

Since our entire patients underwent surgical extirpation irrespective of biopsy outcome, the data comparing the biopsy outcome with final histopathological outcome is more reliable. Most of the studies mentioned in the **table 10** are on active surveillance hence these studies actually compare the biopsy outcome with radiological imaging. This is a major confounding factor in interpretation of these studies.

Advances in cytologic techniques, have contributed to the increasing ability to differentiate between benign and different RCC subtypes using percutaneous renal tumor biopsy .The sensitivities, specificities, PPVs, and NPVs of FNAC and core biopsy for the detection of RCC found in the current study are at the higher end of reported series.(table 10). Overall, most studies have been retrospective, with highly selected patient cohorts and no standardized biopsy protocols. The reported sensitivity of biopsy for the diagnosis of malignancy ranges from 80% to 92%, regardless of the needle size used or whether the specimens were examined cytologically, histologically, or both (116). False-negative results are most often due to a failure to place the needle tip accurately in a small mass. In the current study only about 8% of percutaneous biopsies showed false-negative results. In the retrospective study by Maturen et al, 4% of biopsies were nondiagnostic, and 5% of samples overall were inconclusive in the series.

Exciting advances in immunocytogeneticsand the emergence of reliable markers for identifying specific renal neoplasms, hold great promise for image guided biopsies.(117). These

analyses have the potential for reducing the incidence of non-informative biopsies and providing increased differentiation of “oncocytic neoplasms”

One example of this is the study from Beland *et al* who analyzed RMS that were non-informative by conventional hematoxylin–eosin staining alone, and reported a definitive diagnosis in 89% of cases with the addition of immunohistochemistry and other ancillary techniques. (53). The major diagnostic challenge is represented by oncocytomas. Oncocytic cells are found in numerous RCCs, such as chromophobe RCC, the granular cell variant of RCC, and the eosinophilic variant of papillary type RCC (type 2). Immunocytochemistry can help to distinguish between RCC and oncocytomas. **In this series, only 2 of the 3 patients in whom oncocytic neoplasm was diagnosed on IGB, final histopath came as oncocytoma biopsies. There was possibility of missing one chromophobe RCC if we have not offer surgical extirpation irrespective of biopsy report**. Angiomyolipomas are considered difficult to identify on biopsy due to nuclear atypia and pleomorphism comparable to those found in RCC (117). However HMB-45 is constantly expressed by angiomyolipomas but not by RCC or liposarcomas. Additionally, angiomyolipomas are negative for cytokeratin (118). **In this study so far we have seen only one lipid poor angiomyolipoma in which the IGB was non informative.** The series of Neuzillet et al (35) included 10 oncocytomas, three angiomyolipomas, and one cystadenoma.

We are able to diagnose subtype of renal cancer in 20 of the 22 patient.(90%). Barocas et al (43) was able to improve the accuracy of sub typing from 90% to 95% by adding molecular diagnosis (in which RNA from core biopsies was extracted and quantitative

real-time polymerase chain reaction performed for four gene products to differentiate RCC subtypes) to histopathologic diagnosis. Subtypes of RCC have distinct cytogenetic

abnormalities, such as the loss of 3p in clear-cell, trisomy 7 or 17 in papillary, and widespread chromosomal losses in chromophobe RCC (24, 35, 53). In a recent study by Gowrishankar B(119) et al lends support for a role of a novel FISH assay to assist in the yield and accuracy of diagnosis of renal cortical neoplasms in needle biopsies, in particular to help guide clinical management of patients with SRMs that were non-diagnostic by histology.

Sensitivity is lower than the figures quoted for "accuracy", because it takes into account non-informative biopsies that failed to diagnose the malignancy. The accuracy quoted in many recent studies is unrealistically high. The sensitivity of contemporary RMS series ranges from 84.3% to 100% [Table 10]. Positive predictive value is extremely high in these series as reflected by the very low false-positive rate. Hence, a diagnosis of cancer can be relied on and will almost always be confirmed as malignant on final surgical pathology. **The present study showed the accuracy, sensitivity and positive predictive value to diagnose malignancy were 100%, 95% and 100% respectively.**

Data about negative predictive value must be considered limited, because most patients with a benign diagnosis on RMS do not proceed to surgery. **We have found the negative predictive value to be somewhat low to about 66%.** This is because of failure to differentiate chromophobe RCC from oncocytoma. Data from the Liu et al (28) study indicates that this will be approximately 80–90%. Specificity is often discussed in the RMS literature, but again, conclusions about this should be restricted as a result of the lack of surgical confirmation in most studies.

In summary, the RMS literature to date has been compromised by ambiguous terminology, as well as unclear and at times inappropriate definitions. Quoted "accuracy" rates

may be artifactually high, as RMS is still challenged with major concerns with respect to sampling error, tumor heterogeneity, and presence of “oncocytic neoplasm”. Sensitivity and positive predictive value remains very high overall, and most importantly, false negative rates are almost negligible, which has great clinical relevance. Non-informative biopsies still represent 10–20% of all RMS, although with appropriate recognition, they can be managed in a sensible manner.

Accuracy of tumor grade and subtype

As experience with image guided biopsies is increased, so has interest in the grading of biopsies, because this may have implications for tumor management by stratifying tumor risk. Concordance rates between biopsy specimens and final surgical pathology range from 46% to 94% for Fuhrman nuclear grade,(33,34,54,58). Although most discordant cases are only one grade off. In Lebret study concordance was increased to 7% by compressing the classification to “low” and “high” grade, which is likely to have clinical relevance. This divergence may be a result of both inter observer variability and tumor heterogeneity. The significance of this becomes apparent with the increasing use of active surveillance and ablative therapies, which generally should not be utilized in the setting of a high-grade cancer, regardless of size. (59)

In the present study the concordance between the core biopsy to final histology is 75%. Most of the divergence in nuclear grade is by 1 grade. It is also noticed the present study that probability of reporting low grade in high grade tumour is less than vice versa.

Neuzillet et al (35), investigating 88 biopsies performed with CT guidance and 18-gauge needles in small solid masses, reported a concordance of Fuhrman nuclear grade in

percutaneous biopsy and histopathologic specimens of only 69.8%. In our study the accuracy for detecting high and low Fuhrman grade was 75%. Because Fuhrman grade is a prognostic marker, improvements are needed for a better classification of nuclear grade on biopsy specimens.

As secondary outcome we tried to see if any there is correlation between renal nephrometry score and biopsies, but we failed to identify any concrete correlation.

Conclusion

The role of RMB in the setting of T 1 renal masses is expanding. Approximately 12% of renal masses removed by surgical excision have benign pathology hence surgery can be safely differed if we know pathology beforehand using IGB.

We are able to obtain average 3.6 adequate cores per biopsy. We have noticed that with the above protocol we are able to get adequate tissue in about 92% cases.

The present study showed the accuracy, sensitivity and positive predictive value to diagnose malignancy were 100%, 95% and 100% respectively. We are able to diagnose subtype of renal cancer in 20 of the 22 patient (90%).

Since we have compared the biopsy outcome with final histological outcome the negative predictive value and specificity has more importance. We have found the negative predictive value and specificity to be 66% and 100% respectively. Ongoing research continues to show promise in the development of molecular, cytologic and histologic markers to further characterize renal masses. It might help us in determining optimal immunotherapy in future or targeted systemic therapy susceptibility, predict tumor behaviour and outcomes and discover new pathways in renal tumor biology.

In the present study the concordance between the core biopsy to final histology is 75%. Most of the divergence in nuclear grade is by 1 grade. It is also noticed the present study that probability of reporting low grade in high grade tumour is less than vice versa. Clinicians can increasingly risk-stratify patients based upon RMB results, leading to important decisions such as whether to excise the tumor, likely safety of active surveillance.

Post procedure complications are relatively uncommon, encouraging us for its wider adoption.

If IGB is incorporated in the routine evaluation, physicians will become increasingly skilled at this procedure, thereby decreasing failed biopsy rates.

With this ever increasing data on the usefulness of RMB, it may be time to increase utilization as part of routine practice in the management of the renal masses.

Bibliography

1. Bosniak MA. The small (less than or equal to 3.0 cm) renal parenchymal tumor: detection, diagnosis, and controversies. Radiology. 1991 May;179(2):307–17.

2. Bosniak MA. The current radiological approach to renal cysts. Radiology. 1986 Jan;158(1):1–10.

3. Jemal A, Siegel R, Xu J, Ward E. Cancer statistics, 2010. CA Cancer J Clin. 2010 Oct;60(5):277–300.

4. Bosniak MA, Megibow AJ, Hulnick DH, Horii S, Raghavendra BN. CT diagnosis of renal angiomyolipoma: the importance of detecting small amounts of fat. AJR Am J Roentgenol. 1988 Sep;151(3):497–501.

5. Gill IS, Aron M, Gervais DA, Jewett MAS. Clinical practice. Small renal mass. N Engl J Med. 2010 Feb 18;362(7):624–34.

6. Bosniak MA. Angiomyolipoma (hamartoma) of the kidney: a preoperative diagnosis is possible in virtually every case. Urol Radiol. 1981;3(3):135–42.

7. Zagoria RJ. Imaging of small renal masses: a medical success story. AJR Am J Roentgenol. 2000 Oct;175(4):945–55.

8. Wood BJ, Khan MA, McGovern F, Harisinghani M, Hahn PF, Mueller PR. Imaging guided biopsy of renal masses: indications, accuracy and impact on clinical management. J Urol. 1999 May;161(5):1470–4.

9. acspc-027765.pdf [Internet]. [cited 2014 Mar 26]. Available from: http://www.cancer.org/acs/groups/content/@epidemiologysurveilance/documents/document/acspc-027765.pdf

10. Frank I, Blute ML, Cheville JC, Lohse CM, Weaver AL, Zincke H. Solid renal tumors: an analysis of pathological features related to tumor size. J Urol. 2003 Dec;170(6 Pt 1):2217–20.

11. Nguyen MM, Gill IS. Effect of renal cancer size on the prevalence of metastasis at diagnosis and mortality. J Urol. 2009 Mar;181(3):1020–1027; discussion 1027.

12. Kim JK, Park S-Y, Shon J-H, Cho K-S. Angiomyolipoma with minimal fat: differentiation from renal cell carcinoma at biphasic helical CT. Radiology. 2004 Mar;230(3):677–84.

13. Rodríguez-Rubio FI, Díez-Caballero F, Martín-Marquina A, Abad JI, Berián JM. Incidentally detected renal cell carcinoma. Br J Urol. 1996 Jul;78(1):29–32.

14. Motzer RJ, Bander NH, Nanus DM. Renal-cell carcinoma. N Engl J Med. 1996 Sep 19;335(12):865–75.

15. Homma Y, Kawabe K, Kitamura T, Nishimura Y, Shinohara M, Kondo Y, et al. Increased incidental detection and reduced mortality in renal cancer--recent retrospective analysis at eight institutions. Int J Urol Off J Jpn Urol Assoc. 1995 May;2(2):77–80.

16. Curry NS, Reinig J, Schabel SI, Ross P, Vujic I, Gobien RP. An evaluation of the effectiveness of CT vs. other imaging modalities in the diagnosis of atypical renal masses. Invest Radiol. 1984 Oct;19(5):447–54.

17. Thompson IM, Peek M. Improvement in survival of patients with renal cell carcinoma--the role of the serendipitously detected tumor. J Urol. 1988 Sep;140(3):487–90.

18. Truong LD, Todd TD, Dhurandhar B, Ramzy I. Fine-needle aspiration of renal masses in adults: analysis of results and diagnostic problems in 108 cases. Diagn Cytopathol. 1999 Jun;20(6):339–49.

19. Hollingsworth JM, Miller DC, Daignault S, Hollenbeck BK. Rising incidence of small renal masses: a need to reassess treatment effect. J Natl Cancer Inst. 2006 Sep 20;98(18):1331–4.

20. Lane BR, Babineau D, Kattan MW, Novick AC, Gill IS, Zhou M, et al. A preoperative prognostic nomogram for solid enhancing renal tumors 7 cm or less amenable to partial nephrectomy. J Urol. 2007 Aug;178(2):429–34.

21. Jeldres C, Sun M, Liberman D, Lughezzani G, de la Taille A, Tostain J, et al. Can renal mass biopsy assessment of tumor grade be safely substituted for by a predictive model? J Urol. 2009 Dec;182(6):2585–9.

22. Abouassaly R, Lane BR, Novick AC. Active surveillance of renal masses in elderly patients. J Urol. 2008 Aug;180(2):505–508; discussion 508–509.

23. Volpe A, Jewett MAS. The natural history of small renal masses. Nat Clin Pract Urol. 2005 Aug;2(8):384–90.

24. Lechevallier E, André M, Barriol D, Daniel L, Eghazarian C, De Fromont M, et al. Fine-needle percutaneous biopsy of renal masses with helical CT guidance. Radiology. 2000 Aug;216(2):506–10.

25. Helm CW, Burwood RJ, Harrison NW, Melcher DH. Aspiration cytology of solid renal tumours. Br J Urol. 1983 Jun;55(3):249–53.

26. Murphy WM, Zambroni BR, Emerson LD, Moinuddin S, Lee LH. Aspiration biopsy of the kidney. Simultaneous collection of cytologic and histologic specimens. Cancer. 1985 Jul 1;56(1):200–5.

27. Renshaw AA, Lee KR, Madge R, Granter SR. Accuracy of fine needle aspiration in distinguishing subtypes of renal cell carcinoma. Acta Cytol. 1997 Aug;41(4):987–94.

28. Liu J, Fanning CV. Can renal oncocytomas be distinguished from renal cell carcinoma on fine-needle aspiration specimens? A study of conventional smears in conjunction with ancillary studies. Cancer. 2001 Dec 25;93(6):390–7.

29. Gupta RK, Nowitz M, Wakefield SJ. Fine-needle aspiration cytology of renal angiomyolipoma: report of a case with immunocytochemical and electron microscopic findings. Diagn Cytopathol. 1998 Apr;18(4):297–300.

30. Zhou M, Roma A, Magi-Galluzzi C. The usefulness of immunohistochemical markers in the differential diagnosis of renal neoplasms. Clin Lab Med. 2005 Jun;25(2):247–57.

31. Bonzanini M, Pea M, Martignoni G, Zamboni G, Capelli P, Bernardello F, et al. Preoperative diagnosis of renal angiomyolipoma: fine needle aspiration cytology and immunocytochemical characterization. Pathology (Phila). 1994 Apr;26(2):170–5.

32. Johnson PT, Nazarian LN, Feld RI, Needleman L, Lev-Toaff AS, Segal SR, et al. Sonographically guided renal mass biopsy: indications and efficacy. J Ultrasound Med Off J Am Inst Ultrasound Med. 2001 Jul;20(7):749–753; quiz 755.

33. Volpe A, Kachura JR, Geddie WR, Evans AJ, Gharajeh A, Saravanan A, et al. Techniques, safety and accuracy of sampling of renal tumors by fine needle aspiration and core biopsy. J Urol. 2007 Aug;178(2):379–86.

34. Schmidbauer J, Remzi M, Memarsadeghi M, Haitel A, Klingler HC, Katzenbeisser D, et al. Diagnostic accuracy of computed tomography-guided percutaneous biopsy of renal masses. Eur Urol. 2008 May;53(5):1003–11.

35. Neuzillet Y, Lechevallier E, Andre M, Daniel L, Coulange C. Accuracy and clinical role of fine needle percutaneous biopsy with computerized tomography guidance of small (less than 4.0 cm) renal masses. J Urol. 2004 May;171(5):1802–5.

36. Haber G-P, Colombo JR, Remer E, O'Malley C, Ukimura O, Magi-Galluzzi C, et al. Synchronized real-time ultrasonography and three-dimensional computed tomography scan navigation during percutaneous renal cryoablation in a porcine model. J Endourol Endourol Soc. 2010 Mar;24(3):333–7.

37. Lu DS, Silverman SG, Raman SS. MR-guided therapy. Applications in the abdomen. Magn Reson Imaging Clin N Am. 1999 May;7(2):337–48.

38. Richter F, Kasabian NG, Irwin RJ Jr, Watson RA, Lang EK. Accuracy of diagnosis by guided biopsy of renal mass lesions classified indeterminate by imaging studies. Urology. 2000 Mar;55(3):348–52.

39. Volpe A, Jewett MAS. Current role, techniques and outcomes of percutaneous biopsy of renal tumors. Expert Rev Anticancer Ther. 2009 Jun;9(6):773–83.

40. Masoom S, Venkataraman G, Jensen J, Flanigan RC, Wojcik EM. Renal FNA-based typing of renal masses remains a useful adjunctive modality: evaluation of 31 renal masses with correlative histology. Cytopathol Off J Br Soc Clin Cytol. 2009 Feb;20(1):50–5.

41. Appelbaum AH, Kamba TT, Cohen AS, Qaisi WG, Amirkhan RH. Effectiveness and safety of image-directed biopsies: coaxial technique versus conventional fine-needle aspiration. South Med J. 2002 Feb;95(2):212–7.

42. Hopper KD, Abendroth CS, Sturtz KW, Matthews YL, Shirk SJ. Fine-needle aspiration biopsy for cytopathologic analysis: utility of syringe handles, automated guns, and the nonsuction method. Radiology. 1992 Dec;185(3):819–24.

43. Barocas DA, Mathew S, DelPizzo JJ, Vaughan ED Jr, Sosa RE, Fine RG, et al. Renal cell carcinoma sub-typing by histopathology and fluorescence in situ hybridization on a needle-biopsy specimen. BJU Int. 2007 Feb;99(2):290–5.

44. Schieven LW, Smedts F, Hopman AH, van der Wijk J, Nijman RJ, de Jong IJ. Fine needle aspiration using improved agar microbiopsy is highly concordant with renal mass final diagnosis and subclassification. J Urol. 2009 Dec;182(6):2590–3.

45. Breda A, Treat EG, Haft-Candell L, Leppert JT, Harper JD, Said J, et al. Comparison of accuracy of 14-, 18- and 20-G needles in ex-vivo renal mass biopsy: a prospective, blinded study. BJU Int. 2010 Apr;105(7):940–5.

46. Kümmerlin I, ten Kate F, Smedts F, Horn T, Algaba F, Trias I, et al. Diagnostic problems in the subtyping of renal tumors encountered by five pathologists. Pathol Res Pract. 2009;205(1):27–34.

47. Kümmerlin IPED, Smedts F, ten Kate FJW, Horn T, Algaba F, Trias I, et al. Cytological punctures in the diagnosis of renal tumours: a study on accuracy and reproducibility. Eur Urol. 2009 Jan;55(1):187–95.

48. Lane BR, Samplaski MK, Herts BR, Zhou M, Novick AC, Campbell SC. Renal mass biopsy--a renaissance? J Urol. 2008 Jan;179(1):20–7.

49. Volpe A, Mattar K, Finelli A, Kachura JR, Evans AJ, Geddie WR, et al. Contemporary results of percutaneous biopsy of 100 small renal masses: a single center experience. J Urol. 2008 Dec;180(6):2333–7.

50. Wang R, Wolf JS Jr, Wood DP Jr, Higgins EJ, Hafez KS. Accuracy of percutaneous core biopsy in management of small renal masses. Urology. 2009 Mar;73(3):586–590; discussion 590–591.

51. Caoili EM, Bude RO, Higgins EJ, Hoff DL, Nghiem HV. Evaluation of sonographically guided percutaneous core biopsy of renal masses. AJR Am J Roentgenol. 2002 Aug;179(2):373–8.

52. Vasudevan A, Davies RJ, Shannon BA, Cohen RJ. Incidental renal tumours: the frequency of benign lesions and the role of preoperative core biopsy. BJU Int. 2006 May;97(5):946–9.

53. Beland MD, Mayo-Smith WW, Dupuy DE, Cronan JJ, DeLellis RA. Diagnostic yield of 58 consecutive imaging-guided biopsies of solid renal masses: should we biopsy all that are indeterminate? AJR Am J Roentgenol. 2007 Mar;188(3):792–7.

54. Rybicki FJ, Shu KM, Cibas ES, Fielding JR, vanSonnenberg E, Silverman SG. Percutaneous biopsy of renal masses: sensitivity and negative predictive value stratified by clinical setting and size of masses. AJR Am J Roentgenol. 2003 May;180(5):1281–7.

55. Herts BR, Baker ME. The current role of percutaneous biopsy in the evaluation of renal masses. Semin Urol Oncol. 1995 Nov;13(4):254–61.

56. Nenning H, Rassler J, Minh DH. Heterogeneity of DNA distribution pattern in renal tumours. Anal Cell Pathol J Eur Soc Anal Cell Pathol. 1997;14(1):9–17.

57. Vasselli JR, Shih JH, Iyengar SR, Maranchie J, Riss J, Worrell R, et al. Predicting survival in patients with metastatic kidney cancer by gene-expression profiling in the primary tumor. Proc Natl Acad Sci U S A. 2003 Jun 10;100(12):6958–63.

58. Cajulis RS, Katz RL, Dekmezian R, el-Naggar A, Ro JY. Fine needle aspiration biopsy of renal cell carcinoma. Cytologic parameters and their concordance with histology and flow cytometric data. Acta Cytol. 1993 Jun;37(3):367–72.

59. Lebret T, Poulain JE, Molinie V, Herve JM, Denoux Y, Guth A, et al. Percutaneous core biopsy for renal masses: indications, accuracy and results. J Urol. 2007 Oct;178(4 Pt 1):1184–1188; discussion 1188.

60. Dechet CB, Zincke H, Sebo TJ, King BF, LeRoy AJ, Farrow GM, et al. Prospective analysis of computerized tomography and needle biopsy with permanent sectioning to determine the nature of solid renal masses in adults. J Urol. 2003 Jan;169(1):71–4.

61. Shannon BA, Cohen RJ, de Bruto H, Davies RJ. The value of preoperative needle core biopsy for diagnosing benign lesions among small, incidentally detected renal masses. J Urol. 2008 Oct;180(4):1257–1261; discussion 1261.

62. Tang S, Li JHC, Lui SL, Chan TM, Cheng IKP, Lai KN. Free-hand, ultrasound-guided percutaneous renal biopsy: experience from a single operator. Eur J Radiol. 2002 Jan;41(1):65–9.

63. Tzortzis G, Kolomodi D, Stathopoulou S, Kostakis A, Michail S, Pappas P, et al. Hyperselective renal artery embolisation in the treatment of post-traumatic iatrogenic haematuria: report of two cases. Int Angiol J Int Union Angiol. 1998 Mar;17(1):58–61.

64. Kopecna L, Mach V, Prochazka J. Arteriovenous fistula as a complication of renal biopsy. Bratisl Lekárske Listy. 2005;106(6-7):218–20.

65. Gibbons RP, Bush WH Jr, Burnett LL. Needle tract seeding following aspiration of renal cell carcinoma. J Urol. 1977 Nov;118(5):865–7.

66. Kiser GC, Totonchy M, Barry JM. Needle tract seeding after percutaneous renal adenocarcinoma aspiration. J Urol. 1986 Dec;136(6):1292–3.

67. Shenoy PD, Lakhkar BN, Ghosh MK, Patil UD. Cutaneous seeding of renal carcinoma by Chiba needle aspiration biopsy. Case report. Acta Radiol Stockh Swed 1987. 1991 Jan;32(1):50–2.

68. Abe M, Saitoh M. Selective renal tumour biopsy under ultrasonic guidance. Br J Urol. 1992 Jul;70(1):7–11.

69. ABRAMS HL, SPIRO R, GOLDSTEIN N. Metastases in carcinoma; analysis of 1000 autopsied cases. Cancer. 1950 Jan;3(1):74–85.

70. Bracken RB, Chica G, Johnson DE, Luna M. Secondary renal neoplasms: an autopsy study. South Med J. 1979 Jul;72(7):806–7.

71. Ralls PW, Barakos JA, Kaptein EM, Friedman PE, Fouladian G, Boswell WD, et al. Renal biopsy-related hemorrhage: frequency and comparison of CT and sonography. J Comput Assist Tomogr. 1987 Dec;11(6):1031–4.

72. Sánchez-Ortiz RF, Madsen LT, Bermejo CE, Wen S, Shen Y, Swanson DA, et al. A renal mass in the setting of a nonrenal malignancy: When is a renal tumor biopsy appropriate? Cancer. 2004 Nov 15;101(10):2195–201.

73. Pavlovich CP, Walther MM, Choyke PL, Pautler SE, Chang R, Linehan WM, et al. Percutaneous radio frequency ablation of small renal tumors: initial results. J Urol. 2002 Jan;167(1):10–5.

74. Costa LJ, Drabkin HA. Renal cell carcinoma: new developments in molecular biology and potential for targeted therapies. The oncologist. 2007 Dec;12(12):1404–15.

75. Motzer RJ, Hutson TE, Tomczak P, Michaelson MD, Bukowski RM, Rixe O, et al. Sunitinib versus interferon alfa in metastatic renal-cell carcinoma. N Engl J Med. 2007 Jan 11;356(2):115–24.

76. Escudier B, Eisen T, Stadler WM, Szczylik C, Oudard S, Siebels M, et al. Sorafenib in advanced clear-cell renal-cell carcinoma. N Engl J Med. 2007 Jan 11;356(2):125–34.

77. Demertzis J, Menias CO. State of the art: imaging of renal infections. Emerg Radiol. 2007 Apr;14(1):13–22.

78. Rosenfield AT, Glickman MG, Taylor KJ, Crade M, Hodson J. Acute focal bacterial nephritis (acute lobar nephronia). Radiology. 1979 Sep;132(3):553–61.

79. McKinstry CS. Acute lobar nephronia. Br J Radiol. 1985 Dec;58(696):1217–9.

80. Lee JK, McClennan BL, Melson GL, Stanley RJ. Acute focal bacterial nephritis: emphasis on gray scale sonography and computed tomography. AJR Am J Roentgenol. 1980 Jul;135(1):87–92.

81. Kurowski K. The women with dysuria. Am Fam Physician. 1998 May 1;57(9):2155–64, 2169–70.

82. Silverman SG, Mortele KJ, Tuncali K, Jinzaki M, Cibas ES. Hyperattenuating renal masses: etiologies, pathogenesis, and imaging evaluation. Radiogr Rev Publ Radiol Soc N Am Inc. 2007 Aug;27(4):1131–43.

83. Fielding JR, Visweswaran A, Silverman SG, Granter SR, Renshaw AA. CT and ultrasound features of metanephric adenoma in adults with pathologic correlation. J Comput Assist Tomogr. 1999 Jun;23(3):441–4.

84. Chao DH, Zisman A, Pantuck AJ, Freedland SJ, Said JW, Belldegrun AS. Changing concepts in the management of renal oncocytoma. Urology. 2002 May;59(5):635–42.

85. Jinzaki M, Tanimoto A, Narimatsu Y, Ohkuma K, Kurata T, Shinmoto H, et al. Angiomyolipoma: imaging findings in lesions with minimal fat. Radiology. 1997 Nov;205(2):497–502.

86. Sant GR, Heaney JA, Ucci AA Jr, Sarno RC, Meares EM Jr. Computed tomographic findings in renal angiomyolipoma: an histologic correlation. Urology. 1984 Sep;24(3):293–6.

87. Sherman JL, Hartman DS, Friedman AC, Madewell JE, Davis CJ, Goldman SM. Angiomyolipoma: computed tomographic-pathologic correlation of 17 cases. AJR Am J Roentgenol. 1981 Dec;137(6):1221–6.

88. Shinmoto H, Yuasa Y, Tanimoto A, Narimatsu Y, Jinzaki M, Hiramatsu K, et al. Small renal cell carcinoma: MRI with pathologic correlation. J Magn Reson Imaging JMRI. 1998 Jun;8(3):690–4.

89. Pedrosa I, Chou MT, Ngo L, H Baroni R, Genega EM, Galaburda L, et al. MR classification of renal masses with pathologic correlation. Eur Radiol. 2008 Feb;18(2):365–75.

90. Sussman SK, Glickstein MF, Krzymowski GA. Hypointense renal cell carcinoma: MR imaging with pathologic correlation. Radiology. 1990 Nov;177(2):495–7.

91. Gervais DA, McGovern FJ, Wood BJ, Goldberg SN, McDougal WS, Mueller PR. Radio-frequency ablation of renal cell carcinoma: early clinical experience. Radiology. 2000 Dec;217(3):665–72.

92. Liang P, Wang Y, Zhang D, Yu X, Gao Y, Ni X. Ultrasound guided percutaneous microwave ablation for small renal cancer: initial experience. J Urol. 2008 Sep;180(3):844–848; discussion 848.

93. Mayo-Smith WW, Dupuy DE, Parikh PM, Pezzullo JA, Cronan JJ. Imaging-guided percutaneous radiofrequency ablation of solid renal masses: techniques and outcomes of 38 treatment sessions in 32 consecutive patients. AJR Am J Roentgenol. 2003 Jun;180(6):1503–8.

94. Roy-Choudhury SH, Cast JEI, Cooksey G, Puri S, Breen DJ. Early experience with percutaneous radiofrequency ablation of small solid renal masses. AJR Am J Roentgenol. 2003 Apr;180(4):1055–61.

95. Shingleton WB, Sewell PE Jr. Percutaneous renal tumor cryoablation with magnetic resonance imaging guidance. J Urol. 2001 Mar;165(3):773–6.

96. Silverman SG, Tuncali K, vanSonnenberg E, Morrison PR, Shankar S, Ramaiya N, et al. Renal tumors: MR imaging-guided percutaneous cryotherapy--initial experience in 23 patients. Radiology. 2005 Aug;236(2):716–24.

97. Heilbrun ME, Zagoria RJ, Garvin AJ, Hall MC, Krehbiel K, Southwick A, et al. CT-guided biopsy for the diagnosis of renal tumors before treatment with percutaneous ablation. AJR Am J Roentgenol. 2007 Jun;188(6):1500–5.

98. Tuncali K, vanSonnenberg E, Shankar S, Mortele KJ, Cibas ES, Silverman SG. Evaluation of patients referred for percutaneous ablation of renal tumors: importance of a preprocedural diagnosis. AJR Am J Roentgenol. 2004 Sep;183(3):575–82.

99. Aronson S, Frazier HA, Baluch JD, Hartman DS, Christenson PJ. Cystic renal masses: usefulness of the Bosniak classification. Urol Radiol. 1991;13(2):83–90.

100. Curry NS, Cochran ST, Bissada NK. Cystic renal masses: accurate Bosniak classification requires adequate renal CT. AJR Am J Roentgenol. 2000 Aug;175(2):339–42.

101. Renshaw AA, Granter SR, Cibas ES. Fine-needle aspiration of the adult kidney. Cancer. 1997 Apr 25;81(2):71–88.

102. Harisinghani MG, Maher MM, Gervais DA, McGovern F, Hahn P, Jhaveri K, et al. Incidence of malignancy in complex cystic renal masses (Bosniak category III): should imaging-guided biopsy precede surgery? AJR Am J Roentgenol. 2003 Mar;180(3):755–8.

103. Choyke PL, Glenn GM, Walther MM, Zbar B, Linehan WM. Hereditary renal cancers. Radiology. 2003 Jan;226(1):33–46.

104. Li G, Cuilleron M, Gentil-Perret A, Tostain J. Characteristics of image-detected solid renal masses: implication for optimal treatment. Int J Urol Off J Jpn Urol Assoc. 2004 Feb;11(2):63–7.

105. Lau WK, Blute ML, Weaver AL, Torres VE, Zincke H. Matched comparison of radical nephrectomy vs nephron-sparing surgery in patients with unilateral renal cell carcinoma and a normal contralateral kidney. Mayo Clin Proc. 2000 Dec;75(12):1236–42.

106. Bosniak MA, Rofsky NM. Problems in the detection and characterization of small renal masses. Radiology. 1996 Mar;198(3):638–41.

107. Bosniak MA. Observation of small incidentally detected renal masses. Semin Urol Oncol. 1995 Nov;13(4):267–72.

108. Pospihalj B, Zamparese R, Mazzucchelli R, Morichetti D. Kidney cancer: not a single disease. Anal Quant Cytol Histol Int Acad Cytol Am Soc Cytol. 2007 Dec;29(6):377–9.

109. Rini BI. Metastatic renal cell carcinoma: many treatment options, one patient. J Clin Oncol Off J Am Soc Clin Oncol. 2009 Jul 1;27(19):3225–34.

110. Thomas AA, Rini BI, Campbell SC. Integration of surgery and systemic therapy in the management of metastatic renal cancer. Curr Urol Rep. 2009 Jan;10(1):35–41.

111. Delahunt B, Sika-Paotonu D, Bethwaite PB, William Jordan T, Magi-Galluzzi C, Zhou M, et al. Grading of clear cell renal cell carcinoma should be based on nucleolar prominence. Am J Surg Pathol. 2011 Aug;35(8):1134–9.

112. Pandharipande PV, Gervais DA, Hartman RI, Harisinghani MG, Feldman AS, Mueller PR, et al. Renal mass biopsy to guide treatment decisions for small incidental renal tumors: a cost-effectiveness analysis. Radiology. 2010 Sep;256(3):836–46.

113. Remzi M, Katzenbeisser D, Waldert M, Klingler H-C, Susani M, Memarsadeghi M, et al. Renal tumour size measured radiologically before surgery is an unreliable variable for predicting histopathological features: benign tumours are not necessarily small. BJU Int. 2007 May;99(5):1002–6.

114. Dorffner R, Thurnher S, Prokesch R, Bankier A, Turetschek K, Schmidt A, et al. Embolization of iatrogenic vascular injuries of renal transplants: immediate and follow-up results. Cardiovasc Intervent Radiol. 1998 Apr;21(2):129–34.

115. Maturen KE, Nghiem HV, Caoili EM, Higgins EG, Wolf JS Jr, Wood DP Jr. Renal mass core biopsy: accuracy and impact on clinical management. AJR Am J Roentgenol. 2007 Feb;188(2):563–70.

116. Silverman SG, Gan YU, Mortele KJ, Tuncali K, Cibas ES. Renal masses in the adult patient: the role of percutaneous biopsy. Radiology. 2006 Jul;240(1):6–22.

117. Koul H, Huh J-S, Rove KO, Crompton L, Koul S, Meacham RB, et al. Molecular aspects of renal cell carcinoma: a review. Am J Cancer Res. 2011;1(2):240–54.

118. Nelson CP, Sanda MG. Contemporary diagnosis and management of renal angiomyolipoma. J Urol. 2002 Oct;168(4 Pt 1):1315–25.

119. Gowrishankar B, Cahill L, Arndt AE, Al-Ahmadie H, Lin O, Chadalavada K, et al. Subtyping of renal cortical neoplasms in fine needle aspiration biopsies using a decision tree based on genomic alterations detected by fluorescence in situ hybridization. BJU Int. 2014 Jan 27

name	hospital nuage	sex	side	comorbiditysymptoms			CT finding		number of core obtained	Biopsy outcome	post op biopost biopsyDetails of surgical procedure								post operative details								
mantosh D	494728f	58	m	left	1,2	2	2.2	interpolar	1	2	clear cell gr	1	1--4	2	180	3	3	3	0	0	0	0	0	150			
geeta baur	391977f	49	m	right	6	1	2.3	interpolar	1	6a	2	tissue inadequate	oncocytom	1,2	1	2	140(18)	1	2	0	0	0	0	0	100			
prakash sir	663308f	83	m	left	2	4	2.4	lower	1	5x	2	inconclusive	oncocytom	1	1	2	130	2	2		0	0	2	3	200			
shyamlal sa	438516f	45	m	right	0	2	2.6	lower	1	6x		papillary cell	papillary gr	1,2	02----01	1	120	3	3	0	1	0	0	0	500			
abdul samı	376787f	47	m	left	1,9	2	3	lower	1	4a	2	clear cell grade 1	clear cell g	1,2	1	2	195(45)	1	1		1	0	0	0	500			
Askok kum	274469f	59	m	left	0	2	3	interpolar	1	9a		not conclusive inadequate specimen	chromophc	1,2	1	2	250(20)	1	2	2	1	1		0	600			
gita devi	317158f	45	f	right	5,6	4	3.2	upper	1	8a	3	clear cell grade 1	clear cell g	1	1	1	270(39)	1	1		0	1	0	0	1(500)			
prem kuma	267450f	52	m	left	2	2	3.3	lower	2	5x			clear cell grade 2	4cm	1		90	2	3	0	0	0	0	0	100			
Raja A M	059447a	57	m	right	1,2,5	1	3.3	upper	1	4x		clear cell grade 2	clear cell g	1,,2	1	2	180	2	3	0	0	0	0	0	800			
Deepamani	701258f	29	m	right		1	3.5		1	7a	4	clear cell grade 1	clear cell g	1,2	1	2	180(35)	1	1		1	₀	2	3	1(750)			
md issaq c	628763f	54	m	left	1	1	3.5	lower	1	6p	2	papillary cell	papillary gr	1	1--2	2	130(40)	1	2	0	0	0	0	0	900			
mohd Bela	488504f	30	m	right	2	2	3.6	lower	1	6p	2	clear cell grade 1	clear cell g	1,2	4	2	120	3	3	0	0	0	0	0	100			
balasubran	887531d	53	m	right	1	1	3.8	interpolar	1	9x	2	clear cell grade 2	clear cell g	1,2	4	0	150	3	3	0	0	0		0	500			
sayed iqbal	475130f	35	m	left	0	2	4	upper	1	8p	3	clear cell grade 1	clear cell g	1,2	1	2	240(20)	1	1	0	0	1	0	0	2(2000)			
sunil baran	800764f	36	m	left	0	3	4	upper	1	6x	3	TCC			1	4	2	180	3	3	0	0	0	0	0	100			
anaanda ri	218713f	40	m	right	0	2	4.5	upper	1	6p	2	clearcell grade 1	clear cell g	1,2	2	2	240(23 wa	2	2	0	2	0	0	0	600			
anti pathak	433164F	53	f	left		1	4.8	interpolar	1	10 x		clear cell grade 1	clear cell g	1,2	1	1	135	0	0	0	0	₀	0	0				
sultan Ahm	30569c	59	m	right	1,2	5	5	lower	1	8x	2	clear cell grade 1	clear cell g	1	1	2	150(40)	1	1	0	1	0	0	0	200			
Md Moiz A	221931f	34	m	left	0	3	5.1	lower	1		2	clear cell grade 1	clear cell g	1	1	2	210(40)	1	1	0	1	1	0	0	400			
sartha	308238f	28	f	left	0	1	5.2	interpolar	1	7x		angiomylolipoma																
pradeep sir	679981f	38	m	right	0	1	6	lower	1	9x		chromophobe grade2	chromophc	1,2	1	2	180(20)	3	3	0	1	1	0		800			
gopal chan	673993f	53	m	left	2,5	1	6	interpolar	1	9x	1	clear cell carcinoma	clear cell g	0	1	2	120(10)	1	2	0	1	1		0	200			
karti chand	742103f	60	m	right	0	3	6	interpolar	1	11x	3	papillary grade 1	papillary gr	1	4	2	120	3	3	0	0	0	0	0	50			
parul sarka	106851f	74	m	left	0	1	7	lower	2	10x			clear cell grade 2	6.5	r	4	2	150	3	3	0	0	0	0	0	0	100	
george ver	709647f	54	m	right	2	1 4,2		interpolar	1	6a,5a	3	clear cell grade 2	clear cell g	1	1		240(20)	1	1		1	0	2	0				

DM 1	1 icidental		1 yes
HT 2	2 flank pain		2 no
COPD 3	3 hematuria		
CAD 4	4 other symptoms		
CKD 5	5 LUTS		
anaemia 6			
Other 9			

	1 OPN	1 yes		1 yes	1 cold	1 yes	1 yes	1 plura	1 yes		uneventful	0		1 yes													
1 Pain ₹	2 LPN	2 no		2no	2 warm	2no	2no	2 peritoneu	2no		ICU	vasopressor	1	2	no												
2 Hema	3 ORN			3 not requi	3 not clam	0 not requi	0 not requi	0	no		0 not requi	ICU	ventibion	2	0 not required												
3 Profus	4 LRN											ICU monitoring	3														

4 Arterivenous fistula

5 Pneumothorax, haemothorax

6 Biopsy leading to complication during final surgical procedure